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| 10/763,249      | 01/26/2004  | Naoto Tonouchi       | 247264US0CONT       | 8012             |

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EXAMINER

WALICKA, MALGORZATA A

ART UNIT PAPER NUMBER

1652

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/763,249

Applicant(s)

TONOUCHI ET AL.

Examiner

Malgorzata A. Walicka

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1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1 and 2 is/are allowed.
- 6) ☒ Claim(s) 3-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/01/2006</u> . | 6) <input type="checkbox"/> Other: _____  |

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application Oct.25, 2006, after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Claims 3, 4, 5 and 6 have been amended; claims 35-49 have been cancelled. Claims 1-34 are pending and under examination.

### **DETAILED ACTION**

#### **Priority**

Acknowledgment is made of certified translations of Japanese applications 2001-226568 filed 07/26/2001 and 2001-310547 filed 10/05/2001. However, priority documents do not contain any sequence listing. Thus, the priority of the instant claims to the Japanese applications 2001-226568 filed 07/26/2001 and 2001-310547 filed 10/05/2001 has not been granted.

The instant application is a continuation of the PCT/JP01/07635, filed 07/26/2002. The examiner acknowledges the translation of the priority document that has been published as WO03/10307. The priority of the instant claims to the PCT application has been granted. In results, the instant claims have priority to the filing date of PCT/JP01/07635.

#### **Rejections**

**35 USC, section 112, second paragraph**

Claims 5-6 dependent claims 9-10, 13-14, 17-18, 21-22, 25-26, 29-30, 33-34 were rejected in the office Action of July 25, 2006 (the last action) as being confusing. This rejection is withdrawn, because the claims have been amended.

**35 USC, section 112, first paragraph***Scope of enablement*

Claims 3-4 and dependent claims 5-33 and 34 remain rejected for the reasons explained in the last action. The hybridization conditions of amended claims, i.e., comprising washing at 60 °C and a salt concentration equivalent to 0.1 x SSC and 0.1% SDS, are more stringent than medium stringency conditions which comprise washing at 60 °C and a salt concentration equivalent to 1 x SSC and 0.1% SDS recited by the claims before the current amendment. Still the new hybridization conditions allow for hybridizing DNA having 80%-90% identity; absent a teaching to the contrary. The number of DNA molecules selected moderately stringent conditions is enormously large, thus, one skilled in the art is forced to express this enormously large number of selected DNA molecules and screen the resulting protein molecules for their activity of the peptide forming enzyme, and further select those having the desired activity. In result, as indicated in the last action, the experimentation left to those skilled in the art does not have a high probability of success and is undue.

**Response to Applicants' argument**

In REMARKS, Applicants present their position regarding this rejection:

"It should be noted that the Examiner has failed to provide any reason to doubt the objective truth of enablement of claims containing these stringency conditions", page 12, fourth paragraph.

Applicants argument has been thoroughly considered, but is found not persuasive for the following reasons.

Certainly claiming a DNA which is selected under moderate hybridization condition i.e. having 80% identity, i.e. having about 60 (60 for the sake of simplicity) random mutations in the encoded protein of 330 amino acids ( SEQ ID NO: 15 is 337 amino acid long, (SEQ ID NO: 17 is 323 amino acid long) imposes on a skilled artisan an extremely lengthy experimentation that is undue. Guo et al. 2004 (Protein tolerance to random amino acid change, PNAS, 101/25, 9205-9210, enclosed) teach that the fraction of random single substitution mutations which inactivate a protein of about 300 amino acid (human 3-methyladenine DNA glycosylase) is 0.34 and that this number appears to be consistent with other studies in other proteins as well. Guo et al. further show in Table 1 and formula 1) on page 9206 left column, that the fraction of active mutants for multiple mutations may be roughly estimated by formula  $(1-0.34)^n$  where n is the number of mutations introduced. Applying this estimate to the instant protein having 80%-90% identity, i.e., ~100 mutations of SEQ ID NO: 12, gives only  $(.66)^{60}$  or  $1.5 \times 10^{-11}$  of random mutants being active. Current techniques (i.e., high throughput mutagenesis and screening techniques) in the art would allow for finding a few active mutants within several hundred thousand or up to about a million inactive mutants as is the case for the claims limited to 95% identity (despite even this being an enormous

quantity of experimentation that would take a very long time to accomplish, but finding an appropriated mutant within  $10^{11}$  that are viable would not be possible without undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. Furthermore it is noted that not only is the quantity of experimentation is overwhelming in the instant situation but the specification provides no guidance with regard to what variants to make in order to reduce the amount of experimentation to a reasonable level.

### 3.3. 35 USC section 102

#### Rejection withdrawal

Rejection of claim 1, made in the previous action under 35 U.S.C. 102(b), as being anticipated by *Pseudomonas putida* prolyl aminopeptidase having accession number Q88D01 and disclosed in Nelson K.E. et al., "Complete genome sequence and comparative analysis of the metabolically versatile *Pseudomonas putida* KT2440", *Environ. Microbiol.* 2002, 4, 799-808, is withdrawn, because the claim has been amended.

Rejection of claims 1 and 2, made in the previous action under 35 U.S.C. 102(b), as being anticipated by prolyl aminopeptidase from *Pseudomonas aeruginosa*, having accession number B83010, and disclosed in Stover R. et al., "Complete genome

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sequence of *Pseudomonas aeruginosa* PA01, an opportunistic pathogen, *Nature*, 2000, 406, 959-964, is withdrawn because the claims have been amended.

#### **4. Conclusion**

Claims 3-4 and dependent claims 5-33 and 34 remain rejected, however the claims contain allowable subject matter for the reasons explained in the previous action. Applicants are the first to disclose two enzymes from *Pseudomonas putida* of SEQ ID Nos: 15 and 17, and their encoding DNA of SEQ ID NOs: 14 and 16. No prior art teaches or fairly suggests the enzymes. The enzymes have the application in synthesis of dipeptides.


As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or

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Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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TECHNICAL FIELD: 1652